REMARKS

In an Office Action mailed June 16, 2005 in the above-identified application, the Examiner objected to claims 11-13 as reading on non-elected inventions, rejected claims 12 and 13 as being indefinite, rejected claims 2-4 and 11-13 as failing to comply with the written description and enablement requirements, rejected claims 2-4 and 11-13 as being anticipated by *Bonaldo et al.* and/or *Wu et al.*, and rejected claims 2-4 and 11-13 as containing new matter. The rejections were made final.

Each issue raised by the Examiner is considered separately below. In light of the amendments above and the remarks below, reconsideration is respectfully requested.

No fee is believed to be due in connection with this response. However, if any fee is due in this or any subsequent response, please charge the fee to Deposit Account No. 17-0055.

After Final Practice

The claim amendments provided herein do not introduce any new issue. The amendments to claim 2 limit the claim to certain embodiments within the scope of the claim pending before the amendments. The amendments to claims 6, 7, and 9 also limit the claims to certain embodiments of the claims before the amendments for rejoinder purposes. Claim 11 is amended to track certain embodiments of the claim as originally filed. The office action cited no new art. The subject matter of claims 2-4, 6, 7, 9, and 11-13 has already been considered by the Examiner *vis-a-vis* the same references cited in the office action. Accordingly, this amendment is believed to be appropriate for entry and consideration in after final practice.

Claim Objection

Claims 11-13 are objected to as allegedly drawn to multiple inventions that read on non-elected subject matter. In response, applicants amend claims 11-13 to delete the non-elected subject matter and thereby overcome the objection.

Indefiniteness Rejection under 35 U.S.C. §112, Second Paragraph

The Examiner asserts that claims 12 and 13 recite "a quantitatively predetermined level of expression" but that the metes and bounds of the term are not clear. The term has been deleted from claims 12 and 13 and the rejection is moot.

Written Description Rejection under 35 U.S.C. §112, First Paragraph

Claims 2-4 and 11-13 stand rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement to the extent that the claims encompass (1) nucleic acid molecules with 80% identity to the coding sequence of SEQ ID NO:1 or 3, (2) hybridizing molecules under the recited conditions to the coding sequence of SEQ ID NO:1 or 3, and (3) hybridizing molecules under the recited conditions to a sequence that is 80% identical to the coding sequence of SEQ ID NO:1 or 3. Applicants respectfully traverse the rejection in connection with claims 2-4 and 11-13 as amended.

With respect to the rejected subject matter, claim 2 is amended to only encompass the molecules of (1) and (2) set forth above. The subject matter of (3) described above is deleted from claim 2. Further, claim 11 is amended to encompass an oligonucleotide or a polynucleotide that hybridizes under recited conditions to a coding sequence for SEQ ID NO:2 or SEQ ID NO:4.

Applicants have clearly provided a structural description for the nucleic acid molecules that are at least 80% identical to the coding sequence of SEQ ID NO:1 or 3. With nucleotides 35-859 of SEQ ID NO:1 and nucleotides 1-825 of SEQ ID NO:3 disclosed as the coding sequences in the application, a skilled artisan can certainly envision the exact nucleotide sequences of the nucleic acid molecules that are at least 80% identical to nucleotides 35-859 of SEQ ID NO:1 or nucleotides 1-825 of SEQ ID NO:3. Therefore, these nucleic acid molecules have been described by structure. For any given nucleotide sequence, there is no question whether it is at least 80% identical to nucleotides 35-859 of SEQ ID NO:1 or nucleotides 1-825 of SEQ ID NO:3 and any such sequence falls within the scope of the claims. Accordingly, the written description requirement is satisfied for these nucleic acid molecules.

Similarly, applicants have provided a structural description for nucleic acid molecules that hybridize under the recited conditions to the coding sequence of SEQ ID NO:1 or 3. The specific nucleotide sequences of nucleotides 35-859 of SEQ ID NO:1 and nucleotides 1-825 of SEQ ID NO:3 along with the recited stringent hybridization conditions put a structural limitation (i.e. nucleotide sequence limitation) on the nucleic acid molecules that can hybridize. For example, from the lowest temperature at which only homologous hybridization occurs with a particular concentration of salt (e.g., SSC), 1% mismatching results in about 1°C decrease in the Tm. Therefore, with the specific washing salt concentration and temperature provided, a skilled artisan can readily

determine with reasonable certainty whether any given nucleotide sequence can hybridize to nucleotides 35-859 of SEQ ID NO:1 or nucleotides 1-825 of SEQ ID NO:3 and any such sequence falls within the scope of the claims. In addition, the application provides that these hybridizing nucleic acids are useful as probes for detecting the expression of SEQ ID NO:1 or 3 (see e.g., paragraph [00019], lines 1-5 and paragraph [00028], lines 3-5) and a skilled artisan would clearly recognize that applicants invented these nucleic acid molecules. For the above reasons, the written description requirement for nucleic acid molecules that hybridize under the recited conditions to the coding sequence of SEQ ID NO:1 or 3 is satisfied.

For similar reasons, the written description requirement for an oligonucleotide or polynucleotide that hybridize under recited conditions to a coding sequence for SEQ ID NO:2 or SEQ ID NO:4 is also satisfied.

Enablement Rejection under 35 U.S.C. §112, First Paragraph

Claims 2-4 and 11-13 stand rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement to the extent that the claims encompass (1) nucleic acid molecules with 80% identity to the coding sequence of SEQ ID NO:1 or 3, (2) hybridizing molecules under the recited conditions to the coding sequence of SEQ ID NO:1 or 3, and (3) hybridizing molecules under the recited conditions to a sequence that is 80% identical to the coding sequence of SEQ ID NO:1 or 3. Applicants respectfully traverse the rejection in connection with claims 2-4 and 11-13 as amended.

With respect to the rejected subject matter, claim 2 is amended to only encompass the molecules of (1) and (2) set forth above. The subject matter of (3) described above is deleted from claim 2. Further, claim 11 is amended to encompass an oligonucleotide or a polynucleotide that hybridizes under recited conditions to a coding sequence for SEQ ID NO:2 or SEQ ID NO:4.

Under the enablement requirement, applicants must teach how to make and use the claimed invention. It is well within the capability of a skilled artisan make the nucleic acid molecules at issue and to use them (i) as probes and/or specific controls for detecting the expression of SEQ ID NO:1 or 3 and (ii) as probes for detecting the expression of a SEQ ID NO:2 or 4 coding sequence for generating SEQ ID NO:2 or 4 proteins.

As discussed in the previous section, the application provides that nucleic acid molecules that can hybridize under the recited conditions to the coding sequence of SEQ ID NO:1 or 3 are useful as probes for detecting the expression of SEQ ID NO:1 or 3. Similarly, nucleic acid molecules that are at least 80% identical to the coding sequence of SEQ ID NO:1 or 3 can also be used as probes for determining the expression of SEQ ID NO:1 or 3 when relatively low stringency conditions are used for hybridization or, alternatively, they can be used as specific negative controls for determining the expression of SEQ ID NO:1 or 3 when relatively high stringency conditions are used for hybridization. In addition, any polynucleotide encoding SEQ ID NO:2 or 4 can be provided in an expression vector and introduced into a host cell under suitable conditions to make the protein. A skilled artisan can certainly appreciate that an oligonucleotide or a polynucleotide that hybridizes under the recited conditions to a coding sequence for SEQ ID NO:2 or SEQ ID NO:4 is useful for detecting the expression of the coding sequence and thus help select the right cells for making the protein.

Since it is well with the capability of a skilled artisan to make the nucleic acid molecules at issue and to use them in the applications discussed above, claims 2-4 and 11-13 as amended are enabled.

Anticipation Rejections under 35 U.S.C. §102

The Examiner rejected claims 2-4, 11, and 13 as being anticipated *Bonaldo et al.* and further rejected claims 2 and 11-13 as being anticipated by *Wu et al.* In making the rejections, the Examiner interpreted the term "a coding sequence of SEQ ID NO:1" recited in claims 2 and 11 as encompassing the full length of SEQ ID NO:1, which contains a poly(A) tail, based on the description in the specification that SEQ ID NO:1 encodes a polypeptide of 275 amino acids. As a result, the Examiner asserts that *Bonaldo et al.* anticipate claims 2-4, 11, and 13 as the reference disclosed poly(dT) primers which can hybridize to the poly(A) tail of SEQ ID NO:1. Similarly, the Examiner asserts that *Wu et al.* anticipate claims 2 and 11-13 as the reference disclosed poly (dT) primers and a kit containing positive and negative controls such as liver tumor cells and non-tumor liver cells.

Applicants traverse the Examiner's reading of the claims. It is well established in the art that a "coding sequence" refers only to a sequence that consists of amino acid-specifying codons or the complement thereof. Any nucleic acid that contains a coding sequence for a polypeptide can be said to encode the polypeptide even if the nucleic acid also contains non-coding sequence(s). For example, a gene of a mammalian species in the form of genomic

DNA is said to encode the corresponding protein. However, a skilled artisan understands that this does not mean that the whole genomic DNA is the coding sequence. Only exons but not introns are the coding sequences. It is clearly presented in the sequence listing of the present application that CDS, i.e. the coding sequence, starts at nucleotide 35 and ends at nucleotide 859 with respect to SEQ ID NO:1. A skilled artisan understands that the statement in the specification about SEQ ID NO:1 encoding a polypeptide of 275 amino acids is consistent with the notion that the coding sequence of SEQ ID NO:1 is from nucleotide 35 to nucleotide 859.

As a coding sequence only refers to a sequence that consists of actual codons or the complement thereof and in particular the coding sequence of SEQ ID NO:1 in the present application only refers to nucleotides 35-859, claims 2-4 and 11-13 are not anticipated by *Bonaldo et al.* and/or *Wu et al.*

New Matter Rejection under 35 U.S.C. §112, First Paragraph

The Examiner rejected claims 2-4 and 11-13 alleging that the written description requirement is not satisfied because the newly added limitation "80% identity to the coding sequence of SEQ ID NO:1 or 3" is not supported by the specification.

Applicants respectfully note that the absence of an express description of an added claim limitation is not dispositive for the purpose of the written description requirement and the test is whether the applicant conveyed with reasonable clarity to those skilled in the art that as of the filing date the inventor was in possession of the invention. See *Moba B.V. v. Diamond Automation Inc.*, 325 F.3d 1306 (Fed. Cir. 2003). For example, in *Inverness Medical Switzerland GmbH v. Acon Laboratories Inc.* (D. Mass., No. 03-11323, 4/29/05), which cited the *Moba* case for the above proposition, the court faced the issue whether the written description requirement is satisfied for a claim directed at an immunoassay test device without a casing, which was not expressly described in the specification. The court stated that the question is not whether the specification expressly described a test device operable without a casing, but whether a skilled person in the art would understand from the specification that the applicant had invented a device without casing. Having found that a person skilled in the art would understand from the specification that the casing was not necessary for the device to operate, the court held that the written description requirement is satisfied.

In the present application, although the application does not specifically describe a nucleic acid with 80% identity to the coding sequence of SEQ ID NO:1 or 3, a skilled artisan

would have understood from the application that applicants had possession of the above nucleic acid. Originally filed claims describe a nucleic acid that is at least 80% identical to SEQ ID NO:1 or 3 and the specification along with the sequence listing describe the coding sequences of SEQ ID NO:1 and 3. A skilled artisan clearly understands that the coding sequence of SEQ ID NO:1 or 3 is the most important part of SEQ ID NO:1 and 3. As already discussed in connection with the enablement rejection, a nucleic acid that is at least 80% identical to SEQ ID NO:1 or 3 can be used as a probe for detecting the expression of these sequences. A skilled artisan certainly understands that a polynucleotide that is at least 80% identical to the coding sequence of SEQ ID NO:1 or 3 is also operable as a probe for the same purpose. Therefore, as in *Inverness*, a skilled artisan would have understood from the application that applicants had invented a nucleic acid that is at least 80% identical to the coding sequence of SEQ ID NO:1 or 3 and the written description requirement is thus satisfied for such a nucleic acid.

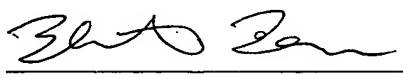
Rejoinder

Previously withdrawn method claims 6, 7, and 9 are amended to incorporate one or more nucleic acids of elected composition claim 2 and they are believed to be eligible for rejoinder in accordance with MPEP 821.04 if claim 2 is found allowable.

Conclusion

Claims 2-4, 6, 7, 9, and 11-13 as amended are believed to be in condition for allowance and a Notice of Allowance is respectfully requested. Should any issue remain outstanding, the Examiner is invited to contact the undersigned at the telephone number appearing below if such would advance the prosecution of this application.

Respectfully submitted,



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